

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
19 February 2004 (19.02.2004)

PCT

(10) International Publication Number
WO 2004/014302 A2

(51) International Patent Classification⁷: **A61K**

(21) International Application Number:
PCT/US2003/024600

(22) International Filing Date: 6 August 2003 (06.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/402,050 9 August 2002 (09.08.2002) US

(71) Applicant and

(72) Inventor: LAW, Peter, K. [US/US]; 2015 Miller Farms Road, Germantown, TN 38138 (US).

(74) Agents: MOTSENBOCKER, MARVIN, A. et al.; Heller Ehrman White & McAuliffe LLP, 1666 K Street, N.W., Suite 300, Washington, DC 20006-1228 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

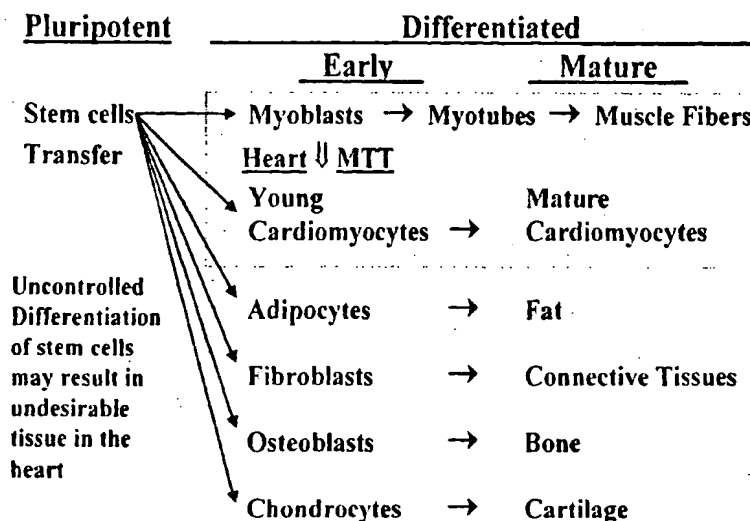
- as to the identity of the inventor (Rule 4.17(i)) for all designations
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

Published:

- without international search report and to be republished upon receipt of that report

[Continued on next page]

(54) Title: MECHANISMS OF MYOBLAST TRANSFER IN TREATING HEART FAILURE



(57) Abstract: Bioengineering the regenerative heart provides a novel treatment for heart failure. On May 14, 2002, a 55-year-old man suffering ischemic myocardial infarction received 25 injections carrying 465 million cGMP-produced *pure* myoblasts into his myocardium after coronary artery bypass grafting. Three myogenesis mechanisms were elucidated with 17 human/porcine xenografts using cyclosporine as immunosuppressant. Some myoblasts developed to become cardiomyocytes. Others transferred their nuclei into host cardiomyocytes through natural cell fusion. As yet others formed skeletal myofibers with satellite cells. *De novo* production of contractile filaments augmented heart contractility. Human myoblasts transduced with VEGF₁₆₅ gene produced six times more capillaries in porcine myocardium than placebo. Xenograft rejection was not observed for up to 20 weeks despite cyclosporine discontinuation at 6 weeks.

WO 2004/014302 A2



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.